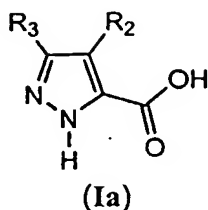


CLAIMS

What is claimed is:

1. A compound of Formula (Ia):



wherein:

R_2 is H, halogen, C_{1-12} alkyl or C_{1-12} haloalkyl; and

R_3 is C_{3-6} cycloalkyl, C_{1-12} alkyl, C_{1-12} haloalkyl, C_{3-6} cycloalkyl- C_{1-4} -alkylene, aryl- C_{1-4} -alkylene or heteroaryl- C_{1-4} -alkylene, wherein said aryl- C_{1-4} -alkylene and heteroaryl- C_{1-4} -alkylene can be optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-4} acyl, C_{1-4} acyloxy, C_{2-4} alkenyl, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} alkylcarboxamide, C_{2-4} alkynyl, C_{1-4} alkylsulfonamide, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, C_{1-4} alkylureyl, amino, C_{1-4} alkylamino, C_{1-4} dialkylamino, arylsulfonyl, carbo- C_{1-4} -alkoxy, carboxamide, carboxy, cyano, C_{3-6} cycloalkyl, C_{1-4} dialkylcarboxamide, C_{1-4} dialkylsulfonamide, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfinyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, heterocyclyl, hydroxyl, thio, nitro, C_{4-6} oxo-cycloalkyl, sulfonamide and sulfonic acid; or a pharmaceutically acceptable salt, solvate or hydrate thereof;

provided that:

- A) if R_2 is H, then R_3 is not CF_3 , *n*-propyl, *iso*-butyl, *n*-butyl, *iso*-propyl, *t*-butyl, methyl, ethyl, *n*-pentyl, *n*-hexyl, *n*-heptyl, *n*-nonyl, *n*-undecyl, *n*-dodecyl, cyclopentyl, benzyl, 4-methyl-benzyl, 4-chloro-benzyl, 4-methoxy-benzyl, 3-chloro-benzyl, phenethyl, or 3-phenyl-propyl;
- B) if R_2 is Cl, then R_3 is not *iso*-butyl, ethyl, or CH_3 ;
- C) if R_2 is Br, then R_3 is not *iso*-butyl, *t*-butyl, or CH_3 ;
- D) if R_2 is I, then R_3 is not CH_3 ;
- E) if R_2 is CH_3 , then R_3 is not CH_3 ; and
- F) if R_2 is CF_3 , then R_3 is not CF_3 .

2. A compound according to claim 1 wherein R_2 is H.

3. A compound according to claim 1 wherein R_2 is halogen.

4. A compound according to claim 3 wherein R_2 is F.
5. A compound according to claim 1 wherein R_2 is C_{1-12} alkyl.
- 5 6. A compound according to claim 5 wherein R_2 is selected from the group consisting of $-CH_3$, $-CH_2CH_3$, $-(CH_2)_2CH_3$, $-(CH_2)_3CH_3$, $-(CH_2)_4CH_3$, and $-(CH_2)_5CH_3$.
7. A compound according to claim 5 wherein R_2 is $-CH_3$ or $-CH_2CH_3$.
- 10 8. A compound according to claim 1 wherein R_2 is C_{1-12} haloalkyl.
9. A compound according to claim 8 wherein R_2 is the haloalkyl selected from the group consisting of $-CHF_2$, $-CH_2F$, $-CH_2CF_3$, $-CH_2CHF_2$, $-CH_2CH_2F$, $-CHFCH_2F$, $-CHFCH_2F$, $-CF_2CH_2F$ and $-CF_2CH_2F$.
- 15 10. A compound according to claim 8 wherein R_2 is $-CHF_2$ or $-CH_2F$.
11. A compound according to claim 8 wherein R_2 is $-CF_3$ or $-CF_2CF_3$.
- 20 12. A compound according to any one of claims 1 to 11 wherein R_3 is C_{1-12} alkyl.
13. A compound according to claim 12 wherein R_3 is selected from the group consisting of $-CH_3$, $-CH_2CH_3$, $-(CH_2)_2CH_3$, $-(CH_2)_3CH_3$, $-(CH_2)_4CH_3$, $-(CH_2)_5CH_3$, $-(CH_2)_6CH_3$, $-(CH_2)_7CH_3$, $-(CH_2)_8CH_3$, $-(CH_2)_9CH_3$, $-(CH_2)_{10}CH_3$, and $-(CH_2)_{11}CH_3$.
- 25 14. A compound according to claim 12 wherein R_3 is selected from the group consisting of $-CH_3$, $-CH_2CH_3$, $-(CH_2)_2CH_3$, or $-(CH_2)_3CH_3$.
15. A compound according to any one of claims 1 to 11 wherein R_3 is C_{1-12} haloalkyl.
- 30 16. A compound according to claim 15 wherein R_3 is C_{1-12} haloalkyl selected from the group consisting of $-CHF_2$, $-CH_2F$, $-CH_2CF_3$, $-CH_2CHF_2$, $-CF_2CH_3$, $-CH_2CH_2CF_3$, $-CH_2CF_2CH_3$, $-CH_2CF_2CF_3$, $-CH_2CH_2CH_2CHF_2$, and $-CH_2CH_2CF_2CH_3$.
- 35 17. A compound according to claim 15 wherein R_3 is C_{1-12} haloalkyl selected from the group consisting of $-CF_3$, $-CF_2CF_3$, and $-(CF_2)_2CF_3$.

18. A compound according to any one of claims 1 to 11 wherein R_3 is C_{3-6} cycloalkyl.
19. A compound according to claim 18 wherein R_3 is cyclopropyl.
- 5 20. A compound according to any one of claims 1 to 11 wherein R_3 is C_{3-6} cycloalkyl- C_{1-4} -alkylene optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, carboxamide, carboxy, cyano, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl, thio, nitro, and sulfonamide.
- 10 21. A compound according to claim 20 wherein said C_{3-6} cycloalkyl- C_{1-4} -alkylene is selected from the group consisting of cyclopropylmethyl, 2-cyclopropyl-ethyl, 1-cyclopropyl-ethyl, 3-cyclopropyl-propyl, 2-cyclopropyl-propyl, 1-cyclopropyl-propyl, 1-cyclopropyl-1-methyl-ethyl, 2-cyclopropyl-1-methyl-ethyl, and 2-cyclopropyl-propyl.
- 15 22. A compound according to claim 20 wherein said C_{3-6} cycloalkyl- C_{1-4} -alkylene is cyclopropylmethyl.
- 20 23. A compound according to any one of claims 1 to 11 wherein R_3 is aryl- C_{1-4} -alkylene optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, carboxamide, carboxy, cyano, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl, thio, nitro, and sulfonamide.
- 25 24. A compound according to claim 23 wherein said aryl- C_{1-4} -alkylene is selected from the group consisting of benzyl, phenethyl, 1-phenyl-ethyl, 3-phenyl-propyl, 2-phenyl-propyl, 1-phenyl-propyl, 1-phenyl-1-methyl-ethyl, 2-phenyl-1-methyl-ethyl, and 2-phenyl-propyl.
- 30 25. A compound according to claim 23 wherein said aryl- C_{1-4} -alkylene is benzyl.
- 35 26. A compound according to any one of claims 1 to 11 wherein R_3 is heteroaryl- C_{1-4} -alkylene optionally substituted with 1 to 5 substituents selected from the group consisting of C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} alkylsulfonyl, C_{1-4} alkylthio, carboxamide, carboxy, cyano, halogen, C_{1-4} haloalkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkylsulfonyl, C_{1-4} haloalkylthio, hydroxyl, thio, nitro, and sulfonamide.

27. A compound according to claim 26 wherein said heteroaryl-C₁₋₄-alkylene is selected from the group consisting of thiophen-2-yl-methyl, thiophen-3-yl-methyl, pyrrol-1-yl-methyl, pyrrol-2-yl-methyl, pyrrol-3-yl-methyl, furan-2-yl-methyl, furan-3-yl-methyl, 2-thiophen-2-yl-ethyl, 2-thiophen-3-yl-ethyl, 2-furan-2-yl-ethyl, 2-furan-3-yl-ethyl, 2-pyrrol-1-yl-ethyl, 2-pyrrol-2-yl-ethyl, and 2-pyrrol-3-yl-ethyl.
28. A compound according to claim 26 wherein said heteroaryl-C₁₋₄-alkylene is selected from the group consisting of thiophen-2-yl-methyl, thiophen-3-yl-methyl, pyrrol-1-yl-methyl, pyrrol-2-yl-methyl, pyrrol-3-yl-methyl, furan-2-yl-methyl, and furan-3-yl-methyl.
29. A compound according to claim 1 wherein said compound is selected from the group consisting of:
- 5-Difluoromethyl-2*H*-pyrazole-3-carboxylic acid;
 - 5-(2,2-Difluoro-ethyl)-2*H*-pyrazole-3-carboxylic acid;
 - 5-(1,1-Difluoro-ethyl)-2*H*-pyrazole-3-carboxylic acid;
 - 5-(2,2-Difluoro-propyl)-2*H*-pyrazole-3-carboxylic acid;
 - 5-(4,4-Difluoro-butyl)-2*H*-pyrazole-3-carboxylic acid;
 - 5-(3,3-Difluoro-butyl)-2*H*-pyrazole-3-carboxylic acid;
 - 5-Cyclopropyl-2*H*-pyrazole-3-carboxylic acid;
 - 5-Cyclopropylmethyl-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-methyl-2*H*-pyrazole-3-carboxylic acid;
 - 5-Difluoromethyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 5-(2,2-Difluoro-ethyl)-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 5-(1,1-Difluoro-ethyl)-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 5-(2,2-Difluoro-propyl)-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 5-Ethyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-propyl-2*H*-pyrazole-3-carboxylic acid;
 - 5-Butyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-pentyl-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-hexyl-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-heptyl-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-octyl-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-nonyl-2*H*-pyrazole-3-carboxylic acid;
 - 5-Decyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
 - 4-Fluoro-5-undecyl-2*H*-pyrazole-3-carboxylic acid;
 - 5-Dodecyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;

5-Cyclopropyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
5-Cyclopropylmethyl-4-fluoro-2*H*-pyrazole-3-carboxylic acid;
5-(3-Fluoro-benzyl)-2*H*-pyrazole-3-carboxylic acid;
5-(3-Bromo-benzyl)-2*H*-pyrazole-3-carboxylic acid;
5-(4-Bromo-benzyl)-2*H*-pyrazole-3-carboxylic acid; and
5-[2-(4-Methoxy-phenyl)-ethyl]-2*H*-pyrazole-3-carboxylic acid.

30. A pharmaceutical composition comprising a compound according to any one of claims 1 to 29 in combination with a pharmaceutically acceptable carrier.
31. A pharmaceutical composition according to claim 30 further comprising an agent selected from the group consisting of α -glucosidase inhibitor, aldose reductase inhibitor, biguanide, HMG-CoA reductase inhibitor, squalene synthesis inhibitor, fibrate, LDL catabolism enhancer, angiotensin converting enzyme inhibitor, insulin secretion enhancer and thiazolidinedione.
32. A compound according to any one of claims 1 to 29 for use in a method of treatment of the human or animal body by therapy.
33. A compound according to any one of claims 1 to 29 for use in a method of treatment of metabolic-related disorders.
34. A compound according to any one of claims 1 to 29 for use in a method of treatment of a metabolic-related disorder selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, obesity, impaired glucose tolerance, atheromatous disease, hypertension, stroke, Syndrome X, heart disease and type 2 diabetes.
35. A compound according to any one of claims 1 to 29 for use in a method of treatment of a metabolic-related disorder selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance and type 2 diabetes.
36. A compound according to any one of claims 1 to 29 for use in a method of treatment of atherosclerosis.

37. A method of treatment of a metabolic-related disorder comprising administering to an individual in need of such treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 29.

5 38. A method according to claim 37 wherein said metabolic-related disorder is selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance and type 2 diabetes.

10 39. A method according to claim 37 wherein said metabolic-related disorder is atherosclerosis.

40. Use of a compound according to one of claims 1 to 29 for the manufacture of a medicament for use in the treatment of a metabolic-related disorder.

15 41. Use of a compound according to one of claims 1 to 29 for the manufacture of a medicament for use in the treatment of a metabolic-related disorder selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, obesity, impaired glucose tolerance, atheromatous disease, hypertension, stroke, Syndrome X, heart disease and type 2 diabetes.

20 42. Use of a compound according to one of claims 1 to 29 for the manufacture of a medicament for use in the treatment of atherosclerosis.